REMARKS

Applicant respectfully requests reconsideration. Claims 3, 4, 8-13, 39, 44, 143, 144, 147 and 149 are pending for examination with claims 3, 13, 39 and 44 being independent claims. Claims 4 and 13 have been amended. No claims have been canceled or added herewith. No new matter has been added.

Rejections under 35 U.S.C. § 112

Claims 3, 4, 8-13, 39, 44, 143, 144, 147 and 149 have been rejected under 35 U.S.C. § 112, first paragraph, for not reasonably providing enablement for decreasing mitochondrial membrane potential in a tumor cell *in vivo*. According to the Examiner, the methods of the claims would result in a generalized response effecting all antigen presenting cells in any part of the body and that the specification and claims do not "disclose a mechanism for, specifically targeting the peptide to the HLA-DR –expressing cells of the tumor without allowing normal antigen presenting cells of the subject to also capture and be affected by the ligand binding to HLA-DR." Applicant traverses the rejection.

The specification provides an enabling disclosure of the claimed method of decreasing mitochondrial membrane potential in a tumor cell (claims 3, 4, 8-12, 39, 143, and 144), decreasing mitochondrial membrane potential in a mammalian cell (claim 13) and for inducing the expression of immune recognition molecules on a cell surface (claims 44, 147 and 149) by contacting the cell with a combination of an HLA-DR inducing agent and an HLA-DR ligand or with a metabolic inhibition agent (claim 44). Each of these concepts is addressed separately below.

The specification discloses methods for decreasing mitochondrial membrane potential in a tumor cell by contacting a tumor cell with an MHC class II HLA-DR inducing agent. It appears from the rejection that the examiner is concerned with the safety of the treatment as a result of non-specific effects on cells other than tumor cells. The rejection is misplaced for several reasons. Firstly, the issue of clinical safety is not a test for enablement. See MPEP 2164.01(c): "The applicant need not demonstrate that the invention is completely safe." In fact, one cannot possibly determine the parameters of safety without a controlled clinical trial, and it is well established that a clinical trial is not required for enablement. "The Federal Circuit has

reiterated that therapeutic utility sufficient under the patent laws is not to be confused with the requirements of the FDA with regard to safety and efficacy of drugs to be marketed in the United States." MPEP 2107.01 III.

Even if safety were relevant to the issue of enablement, at least one of the drugs that are within the class of HLA-DR agents listed in the specification has been administered systemically to patients. For instance, the class of inducing agents includes adriamycin. A discovery of the invention lies in the identification of the induction of the cell surface molecule by regulating the intracellular dissipation of proton motor force using the claimed inducing agents. The cell can then be contacted with the ligand to decrease membrane potential. As far as Applicant is aware, these latter steps were not previously recognized in the art. However, as stated above some inducing agents, such as adriamycin (which, according to the teachings of the invention, has the same biological effects on MHC HLA-DR expression as the inducing agents specifically listed in claims 3 and 39), have previously been administered systemically to patients. Thus, the safety problem proposed by the examiner in the office action has not proven to be a real safety problem that would prevent the systemic administration of an HLA-DR inducing agent.

Claims 3, 4, 8-12, 39, 143, and 144 require that a tumor cell be contacted with the MHC class II HLA-DR inducing agent. These claims do not require that the compound be directed away from other antigen presenting cells. However, methods are well know by those of skill in the art for delivering drugs directly to a tumor site. For instance a drug could be directly injected into a tumor site.

Finally, the specification on pages 59-60 describes methods for delivering a delivery vehicle such as a liposome to target tissue such as the site of a tumor. Thus, to the extent that such a teaching were required for enablement, it can be found within the specification as filed.

Applicant has also claimed methods of inducing the expression of immune recognition molecules on a cell surface by contacting a cell with a metabolic inhibition agent to decrease mitochondrial membrane potential as disclosed in the specification. The cells are not limited to tumor cells. Thus, the reasoning provided in support of the rejection for a lack of enablement, i.e. that applicants have not taught a method for targeting tumor cells exclusively, does not apply to such claims.

Applicant has also claimed a method for decreasing mitochondrial membrane potential in a mammalian cell that is not an antigen presenting cell by contacting the cell with an MHC class

II HLA-DR inducing agent. As discussed above, the specification provides an exemplary teaching of methods for delivering a delivery vehicle such as a liposome to target tissue. Other methods are know to those of skill in the art.

One of ordinary skill in the art would be able to administer the claimed compounds of the invention using no more than routine experimentation with Applicant's disclosure in hand. Accordingly, withdrawal of the rejection of claims 3, 4, 8-13, 39, 44, 143, 144, 147 and 149 under 35 U.S.C. § 112, first paragraph, is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
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